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wherein the ANT polypeptide comprises an amino acid sequence that is at least 95 percent identical to a human ANT3 sequence as set forth in SEQ ID NO:33.

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57. (Amended) The fusion protein of claim 47 wherein the additional polypeptide sequence is a polypeptide having affinity for a ligand.

REMARKS

Reconsideration of the present application in view of the following remarks is respectfully requested. Claims 42, 46-48, 51-53, 56 and 57 are pending. Claims 52, 53 and 56 have been canceled and claims 42, 46, 47, 51 and 57 have been amended in a manner that more clearly defines certain subject matter encompassed by applicants' invention. Support for the amendments may be found in the specification, for example, at page 18, lines 17-19 and page 24, lines 9-13; at page 35, line 17 through page 36, line 11; at page 38, lines 1-10 and at page 71, lines 23-24. Claim 57 has been amended solely to correct an otherwise improper dependency on a canceled claim. No new matter has been added.

Attached hereto is a marked-up version of the changes made to the claims by the current Amendment, the first page of which is captioned "Version with Markings to Show Changes Made."

REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 42, 46-48, 51-53, 56 and 57 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not adequately described in the specification. More specifically, the Action asserts that the specification fails to describe the distinguishing characteristics of each of the claimed genera of isolated adenine nucleotide translocator (ANT) polypeptides, such as human (claims 42, 46-48, 51, 57) or animal (claims 52, 53, 56, 57) ANT polypeptides, or ANT1, ANT2 or ANT3 polypeptides, or ANT polypeptide variants and fragments.

Applicants respectfully traverse these grounds for rejection and submit that the description of the claimed invention in the specification is sufficient to reasonably convey to a person skilled in the art that the applicants, at the time of filing the application, had possession of the claimed invention. The present invention is directed in pertinent part to an isolated recombinant human adenine nucleotide translocator polypeptide comprising an amino acid sequence that is at least 95 percent identical to a human ANT3 sequence as set forth in SEQ ID NO:33 and that localizes to a mitochondrial membrane, that is capable of binding an ANT ligand and that is produced by a method comprising culturing a host cell comprising a recombinant expression construct comprising at least one regulated promoter operably linked to a nucleic acid encoding the adenine nucleotide translocator polypeptide. In certain embodiments the host cell lacks an endogenous human ANT1 adenine nucleotide translocator polypeptide as set forth in SEQ ID NO:31 and also lacks an endogenous human ANT2 adenine nucleotide translocator polypeptide as set forth in SEQ ID NO:32. Also, in view of the amendment submitted herewith, the rejection of claims 52, 53 and 56 is rendered moot such that applicants request it be withdrawn.

Applicants submit that the instant specification adequately describes distinguishing characteristics of the subject invention polypeptides. In particular, the specification teaches the sequence of a representative disclosed species of human ANT3 polypeptide (*see, e.g.*, page 18, lines 17-19; page 24, lines 9-13; SEQ ID NO:33), and also provides for minor variants that comprise amino acid sequences that are at least 95 percent identical to SEQ ID NO:33 (*e.g.*, page 23, line 17 through page 24, line 22), as may be determined according to the present application and through the use of methodologies known to the art, for example, sequence analysis techniques. Applicants submit that as disclosed in the specification and recited in the instant claims, the subject invention human ANT3 polypeptides are clearly described structurally and functionally and can be readily distinguished from other human ANT polypeptides and from ANT polypeptide derived from non-human animals or other life forms. In addition to the sequence-based structural limitation recited by the instant claims, and for reasons previously made of record, the specification provides abundant description of how to make and use an isolated human ANT3 polypeptide that localizes to a mitochondrial membrane, that is capable of binding an ANT ligand and that is produced according to the

recited recombinant method. Accordingly, applicants submit that a person having ordinary skill in the art would recognize that applicants were in possession of the attributes common to the members of the genus.

Therefore, applicants respectfully submit that the instant specification and claims adequately describe the claimed invention and that the requirements of 35 U.S.C. § 112, first paragraph, are satisfied. Accordingly, applicants respectfully request that this rejection be withdrawn.

REJECTIONS UNDER 35 U.S.C. § 102(a)

The Examiner rejected claims 42 and 46 under 35 U.S.C. § 102(a) as being anticipated by Marzo et al. (*Science* 281:2027-2031, 1998). More specifically, the Action asserts that Marzo et al. teach a purified human ANT2 protein. The Action alleges further that applicants' invention is the same product as that described by Marzo et al., but is merely derived via an alternative process.

Applicants respectfully traverse this ground for rejection. As discussed above, the present invention is directed, in pertinent part to an isolated recombinant human adenine nucleotide translocator polypeptide comprising an amino acid sequence that is at least 95 percent identical to a human ANT3 sequence as set forth in SEQ ID NO:33 and having the recited characteristics (e.g., localizes to mitochondria, capable of binding an ANT ligand, etc.).

Applicants submit that the cited reference fails to meet every limitation of the instant claims and, therefore, that Marzo et al. fail to anticipate the claimed invention. More specifically, applicants respectfully submit that Marzo et al. fail to teach an isolated recombinant human ANT3 polypeptide having a sequence that is at least 95% identical to SEQ ID NO:33. Neither do Marzo et al. disclose or in any way contemplate such a polypeptide that is isolated from a host cell that lacks endogenous human ANT1 (SEQ ID NO:31) and ANT2 (SEQ ID NO:32) polypeptides, as claimed according to the present invention.

Applicants respectfully submit that the Action misapplies the reference where it refers to Marzo et al. at page 2029, Column 1, lines 9-32, Fig. 2C and Fig. 4 (Action, page 7, line 7). A careful reading of Marzo et al. reveals that, contrary to the assertion in the Action that

Marzo et al. there disclose a purified human ANT2 protein that “was purified to greater than 95% homogeneity . . .”, the ANT described in Fig. 2C is not a human ANT but is instead derived from rat brain (Marzo et al. at page 2029, Col. 1, line 15), which therefore cannot be human ANT2 as alleged by the Action, and which in any event cannot be an isolated recombinant human ANT polypeptide comprising an amino acid sequence that is at least 95 percent identical to SEQ ID NO:33 according to the instant claims. Furthermore, the Action asserts that Marzo et al., at page 2029, Col. 1, lines 29-31, describe human ANT2 that was purified to greater than 95% homogeneity, but applicants submit that this is in fact a reference to the ANT shown in Fig. 4C, as noted by Marzo et al. at page 2029, Col. 1, lines 32-37, wherein further the legend for Fig. 4C (Marzo et al., page 2030) clearly refers to “purified ANT from rat myocardium”, which again cannot be human ANT2 as alleged by the Action. Figure 4A of Marzo et al. relates to a human ANT from an HT-29 cell, but applicants submit that the ANT of Fig. 4A is not a recombinant human ANT polypeptide having at least 95 percent sequence identity to a human ANT3 sequence as set forth in SEQ ID NO:33 of the present application. Applicants therefore submit that nowhere in Marzo et al. is a polypeptide meeting all the limitations of the presently claimed invention taught or even suggested.

Moreover with respect to recombinant methodologies, Marzo et al. merely describe recombinant expression of a 55 amino acid domain of human ANT2 in an intact yeast dihybrid cell system (Marzo et al., Figure 4B at p. 2030; note 22 at page 2031), and the teachings of Marzo et al. in this regard are limited to detection of protein-protein interactions within such intact cells. Applicants therefore respectfully submit that Marzo et al. fail to teach a recombinant, isolated human ANT3 polypeptide which, as disclosed in the instant specification and as recited in the instant claims, localizes to a mitochondrial membrane, is capable of binding an ANT ligand, and has at least 95 percent sequence identity to SEQ ID NO:33.

Accordingly, the Action fails to show that the prior art products necessarily possess the characteristics of the claimed product and therefore fails to establish a *prima facie* case of anticipation. Moreover, according to section 2112 of the M.P.E.P.:

The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1995, 1997 (Fed. Cir. 1993) (emphasis in original)(MPEP § 2112).

Further, the M.P.E.P. states that:

To establish inherency, the extrinsic evidence ‘must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.’ *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (MPEP § 2112).

Applicants respectfully submit that the Examiner has not met the burden of making it clear that the missing descriptive matter, *i.e.*, whether Marzo et al. disclose an ANT polypeptide comprising an amino acid sequence that is at least 95 percent identical to SEQ ID NO:33, is necessarily present in the cited reference. In fact, the Action asserts that Figures 2C and 4C of Marzo et al. disclose isolated human ANT2, an assertion which must be called into question for reasons given above. The Action also asserts that Fig. 4A teaches what “appears to be full length” ANT which “would be expected” to localize to mitochondrial membranes without pointing to any relevant express disclosure in Marzo et al. because none is to be found therein. As made clear by the M.P.E.P., such conjecture does not suffice as a finding that the prior art reference contains a disclosure that anticipates the presently claimed invention.

In addition, according to section 2131.01 (III) of the M.P.E.P:

To serve as an anticipation when the reference is silent about the asserted inherent characteristics, such gap by the references may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991) (M.P.E.P. § 2131.01 (III)).

Applicants submit that the Action fails to provide evidence or reasoning to overcome the deficiencies of Marzo et al. Accordingly, applicants respectfully submit that the instant invention is readily distinguished over Marzo et al., and request that the rejection under 35 U.S.C. § 102(a) be withdrawn.

The Examiner also rejected claim 46 under 35 U.S.C. § 102(a) as being anticipated by Fiore et al. (*Biochimie* 80:137-150, 1998). More specifically, the Examiner asserts that Fiore *et al.* teach isolation and characterization of mitochondrial ADP/ATP carrier

proteins (ANT proteins), including amino acid sequence alignments of multiple human and animal ANT proteins.

Applicants respectfully traverse this ground for rejection and submit that Fiore et al. fail to anticipate the claimed invention. It is well settled that for a reference to anticipate a claim under 35 U. S. C. §102, the reference must teach every limitation of the claim. Applicants submit that Fiore et al. fail to provide every limitation of the claim, making application of this reference inapposite for rejection under §102. In the instant case, the Action concedes that Fiore et al. provide a review of ANT proteins. Applicants submit, however, that the teachings of Fiore et al. merely refer generally to isolation and characterization of ANT proteins from a variety of sources, but that Fiore et al. do not disclose the present invention. Moreover, Fiore et al. teach that the amino acid sequences of most ANT polypeptides described therein were deduced from nucleotide sequences (page 138, column 2, lines 1-3 under “Genomic Structure of the ADP/ATP Carriers”) without disclosing which ANT polypeptides were isolated. In other words, Fiore et al. nowhere expressly disclose actual isolation of a recombinant human ANT3 polypeptide according to the present invention.

In support of the rejection, the Action points to Fiore et al. at page 138, first column, last four lines, but applicants submit that this passage refers to general properties of ANT polypeptides but fails to teach an isolated *human* ANT3 polypeptide having at least 95% sequence identity to SEQ ID NO:33, as recited by the instant claims, and therefore the disclosure of Fiore et al. fails to meet the limitations of the instant claims. The Action also points to Fiore et al. at page 144, last paragraph, where, concededly, an isolated yeast ANT polypeptide is described. Here again, applicants submit that the Action has failed to point to an anticipating disclosure in the art, where the cited passage fails to provide an isolated *human* ANT3 polypeptide having at least 95% sequence identity to SEQ ID NO:33 according to the present invention. The Action nowhere points to any teaching or suggestion of the present invention in Fiore et al.; applicants therefore submit that the present invention is readily distinguished over the cited reference.

As described in the specification, for example, at page 21, lines 9-15, an “isolated” ANT polypeptide will include an ANT polypeptide that is removed from its original environment. Fiore et al. merely teach that known ANT polypeptide *sequences* (i.e., the

sequence information, but not any isolated human polypeptide) have been deduced from nucleotide coding sequences (page 138, column 2, lines 1-3 under “Genomic Structure of the ADP/ATP Carriers”), but Fiore et al. fail to disclose actual *isolation* of any human ANT polypeptides. Fiore et al. also fail to disclose *isolation* of a recombinant human ANT3 having at least 95% sequence identity to SEQ ID NO:33, or of any recombinant human ANT polypeptide, that localizes to a mitochondrial membrane; Fiore et al. fail to disclose any *isolated* recombinant human ANT3 polypeptide that is capable of binding an ANT ligand; Fiore et al. fail to disclose any *isolated* recombinant human ANT3 polypeptide that is produced by culturing a host cell comprising a recombinant expression construct comprising a regulated promoter operably linked to an ANT3-encoding nucleic acid. Applicants therefore submit that Fiore et al. fail to teach or suggest the subject matter of the instant claims.

Accordingly, applicants respectfully submit that the instant invention is readily distinguished over Fiore et al., and request that the rejection under 35 U.S.C. § 102(a) be withdrawn.

REJECTIONS UNDER 35 U.S.C. § 103(a)

The Examiner rejected claims 42 and 46-57 under 35 U.S.C. § 103(a) as being unpatentable over Fiore et al. (*Biochimie* 80:137-150, 1998) in view of Rosenberg (*Protein Analysis and Purification: Benchtop Techniques*, Birkhäuser, Boston, pp. 335-347, 1996). In particular, the Examiner alleges that Fiore et al. teach full length human ANT *sequences* (but, as applicants have noted above, Fiore et al. teach no actual human ANT polypeptides *per se*), and a yeast ANT fusion protein (but concededly, according to the Action, no human ANT fusion protein), and that Rosenberg describes fusion proteins comprising a protein of interest fused to a marker enzyme or an affinity tag. The Action then asserts that a person having ordinary skill in the art would have found it obvious to express ANT sequences of Fiore et al. as fusion proteins using the fusion partners of Rosenberg, by substituting a human or animal ANT sequence for the yeast ANT sequence of Fiore et al.

The Examiner also rejected claims 42, 46, 47, 51-53, 56 and 57 under 35 U.S.C. § 103(a) as being unpatentable over Adrian et al. (*Mol. Cell. Biol.* 6(2):626-634, 1986), in

view of Fiore *et al.* The Action alleges that Adrian et al. describe amino acid sequence requirements for mitochondrial localization of a yeast ANT fusion protein comprising an enzyme reporter molecule, β -galactosidase. The Action then asserts that it would have been obvious to substitute human ANT provided by the teachings of Fiore et al. for yeast ANT according to Adrian et al., to express human ANT as a β -galactosidase fusion protein. The Examiner further cites Brandolin *et al.* (*Biochemistry* 24: 1991-1997, 1985), a publication cited by Fiore *et al.* (*supra*), as allegedly providing further evidence that isolation of ANT proteins was well known to the art at the time of filing the instant application.

Applicants respectfully traverse these grounds for rejection. The cited references, alone or in combination, fail to teach or suggest an isolated recombinant human adenine nucleotide translocator polypeptide comprising an amino acid sequence that is at least 95 percent identical to a human ANT3 sequence as set forth in SEQ ID NO:33 and that localizes to a mitochondrial membrane and is capable of binding an ANT ligand, or an isolated fusion protein comprising such an adenine translocator polypeptide fused to at least one additional polypeptide sequence. Insofar as the rejections of claims 52, 53 and 56 are rendered moot by cancellation of these claims according to the present amendment, applicants respectfully request that these rejections be withdrawn. Additionally, and with regard to claim 42, applicants submit that the present rejections under 35 U.S.C. §103 are inapposite, where the Action asserts that the combination of references renders obvious a fusion protein but the instant claim is not so limited. Nevertheless, and without acquiescing in the rejection, applicants provide the following remarks in traversal of the rejections of all of the instant claims, including claim 42.

Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness. (*See In re Mayne*, 104 F.3d 133, 1341-43, 41 U.S.P.Q.2d 1451 (Fed. Cir. 1997) (PTO has the burden of showing a *prima facie* case of obviousness.)). The Examiner must show (1) that the combined references teach or suggest all claim limitations; (2) that the references provide some teaching, suggestion, or motivation to combine or modify the teachings of the prior art to produce the claimed invention; and (3) that the combined teachings of the references indicate that by combining the references, a person having ordinary skill in the art will achieve the claimed invention with a reasonable expectation of success. When rejection of claims depends upon a combination of prior art references, a teaching, motivation, or suggestion

to combine the references must exist. (See *In re Rouffet*, 149 F.3d 1350, 1355, 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998)).

Applicants traverse the rejections over Fiore in view of Rosenberg because the cited combination of references would not have motivated a person having ordinary skill in the art to arrive at the claimed invention. By way of contrast, applicants submit that the cited references, if anything, teach away from the present invention. Specifically, Fiore et al. are limited in their teachings of recombinant ANT expression to a yeast expression system that fails to express any non-yeast ANT3 polypeptide other than a single mutant comprising a single amino acid substitution of wild-type yeast ANT 3 (Anc2p, Fiore et al. page 138, 2nd column, lines 19—29; cf. Fiore et al., page 144, 1st column, last paragraph), while Rosenberg (which is merely cumulative subject matter, for reasons already made of record) disclose fusion protein solubilization methodologies that require high concentrations of chaotropic agents (e.g., 8M guanidine, Rosenberg p. 339; 5M guanidinium, p. 340) to provide negligible yields (e.g., only ~1% of total fusion protein solubilized, Rosenberg, p. 339).

Applicants therefore respectfully submit that the Action errs in alleging that based on this combination an ordinarily skilled artisan would have been motivated to obtain “easier purification” (Action, p. 11, lines 17-18) to arrive at the presently claimed invention with any reasonable expectation of success. If anything, applicants submit that the combination of the cited references fails to provide the requisite motivation where the artisan would recognize that subtle changes in an ANT polypeptide sequence may preclude successful expression of the ANT, and where further the artisan would appreciate that denaturation of ANT polypeptides by chaotropes is not necessarily reversible in a manner that would restore requisite function of a conformation-sensitive protein, absent any evidence. Applicants therefore respectfully submit that in alleging that there would have been motivation to combine the references to achieve “easier purification”, the Action asserts nothing more than that it would have been “obvious to try” to improve on the prior art methods. Such an assertion cannot be regarded as a conclusory finding that the claimed invention is obvious, and in fact fails to support a *prima facie* case of obviousness. *In re Eli Lilly & Co.*, 902 F.2d 943; 14 USPQ2d 1741 (Fed. Cir. 1990).

Similarly, applicants submit that the Action employs inappropriate and selective hindsight where the allegation of obviousness is asserted to derive from a reason or suggestion in

the art other than knowledge provided by applicants' disclosure. *In re Dow Chemical Co.*, 837 F.2d 469; 5 USPQ2d 1529 (Fed. Cir. 1988).

In particular, the present application discloses (e.g., page 44, line 21 through page 45, line 16, including incorporated references cited therein), and the art well knows (e.g., Fiore et al., pp. 143-44; Brandolin et al., 1997, cited in the Action), that ANT activity is highly conformation-dependent, while a chaotropic agent such as 5-8M guanidine according to Rosenberg is known to disrupt protein conformation in a manner that is not necessarily reversible. As noted above with reference to M.P.E.P. §§2112 and 2131.01, extrinsic evidence is required where the cited reference fails to unambiguously anticipate the claimed invention. Here, the Action fails to meet its burden of providing evidence that a person ordinarily skilled in the art would reasonably expect the chaotropes of Rosenberg to reversibly denature the claimed human ANT3 polypeptides in a manner that would preserve or restore the recited functional characteristics of ligand binding and membrane localization.

Moreover, where the teaching of Fiore et al. (p. 138 and p. 144, as cited *supra*; Fiore et al. obtained a fusion protein only using the single amino acid-substituted Anc2p) is limited to the disclosure that the yeast ANT expression system described therein would not tolerate any mutation in yeast ANT3 beyond a single amino acid substitution, applicants submit the ordinarily skilled artisan would not reasonably expect to successfully obtain a highly heterologous recombinant ANT3, namely a recombinant human ANT3 polypeptide having a sequence at least 95 percent identical to SEQ ID NO:33. Applicants therefore submit that therefore it would not be at all reasonable to expect to achieve successfully the claimed recombinant human ANT3 polypeptides or fusion proteins having the recited characteristics, e.g., ligand binding and mitochondrial membrane localization, where potentially inappropriate sequences and methodologies that would compromise the function of the product are all that the prior art suggests. A claimed invention cannot be *prima facie* obvious if the combination of references asserted in the Action would render such modification of the prior art inoperative. *In re Sponnoble*, 405 F.2d 578; 160 USPQ 237 (1969 C.C.P.A.).

Applicants have noted, and respectfully traverse, the assertions in the Action regarding secondary considerations, and wish to hold these assertions in abeyance until such time as it can be determined whether the present amendment has obviated any need for submission of

an appropriate declaration directed to these issues. Applicants submit that Miroux et al. is merely representative of, and not the extent of, evidence indicating that despite sustained efforts in the art, a recombinant human ANT3 polypeptide having the recited characteristics according to the instant claims could not be isolated at the time of filing the instant application.

Applicants also respectfully submit that the combination of Adrian et al. in view of Fiore et al. fails to teach or suggest each and every limitation of the present invention. The disclosure of Adrian et al. is limited to a determination of whether yeast ANT shares mitochondrial targeting sequence motifs with other typical mitochondrial proteins using three truncated deletion mutants of yeast ANT, the largest of which comprises 281 amino acids out of the 309 amino acids which comprise the full length yeast ANT, but Adrian et al. fail to contemplate in any way the recombinant expression of human ANT3 polypeptides that are 95 percent identical to SEQ ID NO:33 and that are capable of binding to an ANT ligand according to the present invention. Contrary to the assertion in the Action, the present invention does not pertain to recognition by applicants of “another advantage which would flow naturally” from the prior art; instead, the cited references teach away from the present invention and would not provide the requisite motivation to the ordinarily skilled artisan.

More specifically, Adrian et al. disclose a truncated yeast ANT polypeptide that includes all four transmembrane domains yet apparently lacks ANT ligand binding activity, while Fiore et al., as discussed above, suggest that yeast ANT sequences which deviate from wildtype yeast ANT by more than the most trivial amino acid substitutions are not likely to be successfully expressed. An alignment of the yeast (“ScAnc2”) and human (“HuAnc2”) ANT3 sequences as presented in Fiore et al. shows six substitutions just in the region corresponding to amino acids 78-98 of the yeast protein, which region Adrian et al. describe as important to mitochondrial membrane localization (a recited characteristic of the instant claims) of ANT polypeptides (Adrian et al., page 633, 2nd column, 1st full paragraph). Combined with the teachings of Fiore et al. as discussed above, that ANT ligand binding by ANT polypeptides (also a recited characteristic of the instant claims) is conformation dependent, and that ANT3 polypeptide expression in yeast does not appear to tolerate radical alterations to the ANT3 polypeptide amino acid sequence, applicants submit that a person having ordinary skill in the art

would not reasonably expect to succeed in arriving at the presently claimed invention. Thus, where the prior art failed to suggest to the person having ordinary skill in the art that the presently claimed human ANT3 polypeptides should be made according to the present invention, and where, for reasons discussed herein, such a skilled artisan would not have been provided with a reasonable expectation of success in doing so based on the prior art, applicants submit that *prima facie* obviousness has not been established. *See, e.g., In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Applicants therefore respectfully submit that the Action has not set forth a *prima facie* case of obviousness, and respectfully request that these rejections be withdrawn.

REJECTIONS UNDER 35 U.S.C. § 101

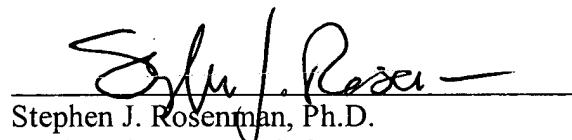
The Examiner also provisionally rejected claims 42, 46-48, 51-53 and 56-57 under 35 U.S.C. § 101, for alleged double patenting in view of co-pending Application No. 09/185,904.

Applicants respectfully traverse this rejection. The rejections of claims 46, 52, 53 and 56 are obviated by the cancellation of these claims according to the amendment submitted herewith. With regard to the remaining instant claims, applicants submit that the provisional double patenting rejection has been rendered moot by the present amendment, according to which the allegedly conflicting claims are no longer coextensive in scope. In particular, and as discussed above, the claims of the instant application are directed in pertinent part to a human ANT3 polypeptide having a sequence that is at least 95 percent identical to SEQ ID NO:33, while the subject matter of the cited copending application is not so limited. As this is a provisional rejection, at such time as the instant claims are in otherwise allowable condition, applicants reserve the right to further amend and/or to cancel one or more claims in the present application and/or in co-pending Application No. 09/185,904 without prejudice to either application or to any related continuation, divisional, continuation-in-part, reissue or reexamination application.

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited. If the Examiner does not believe the claims are allowable for any reason, the Examiner is encouraged to telephone the undersigned at (206) 622-4900.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC



Stephen J. Rosenman, Ph.D.
Registration No. 43,058

SJR:kw

Enclosure:
Postcard

701 Fifth Avenue, Suite 6300
Seattle, Washington 98104-7092
Phone: (206) 622-4900
Fax: (206) 682-6031

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Version with Markings to Show Changes Made

Claims 52, 53 and 56 have been canceled without prejudice..

Claims 42, 46, 47, 51 and 57 to read as follows:

42. (Twice Amended) An isolated recombinant human adenine nucleotide translocator polypeptide comprising an amino acid sequence that is at least 95 percent identical to a human ANT3 sequence as set forth in SEQ ID NO:33 and that localizes to a mitochondrial membrane, that is capable of binding an ANT ligand and that is produced by a method comprising culturing a host cell comprising a recombinant expression construct comprising at least one regulated promoter operably linked to a nucleic acid encoding the adenine nucleotide translocator polypeptide.

46. (Twice Amended) The isolated polypeptide of claim 42 wherein the host cell lacks an endogenous human ANT1 adenine nucleotide translocator polypeptide as set forth in SEQ ID NO:31 and wherein the host cell lacks an endogenous human ANT2 adenine nucleotide translocator polypeptide as set forth in SEQ ID NO:32 ~~is recombinant ANT3 or a variant or fragment thereof.~~

47. (Twice Amended) An isolated recombinant human adenine nucleotide translocator fusion protein comprising an adenine translocator polypeptide fused to at least one additional polypeptide sequence, wherein the ANT polypeptide comprises an amino acid sequence that is at least 95 percent identical to a human ANT3 sequence as set forth in SEQ ID NO:33 and wherein the fusion protein localizes to a mitochondrial membrane and is capable of binding an ANT ligand.

48. The fusion protein of claim 47 wherein said one additional polypeptide sequence is an enzyme sequence or a variant or fragment thereof.

51. (Twice Amended) An isolated human adenine nucleotide translocator fusion protein comprising an adenine translocator polypeptide fused to at least one additional polypeptide sequence cleavable by a protease that separates the adenine translocator polypeptide from the remainder of the fusion protein, said adenine nucleotide translocator polypeptide being capable of localizing to a mitochondrial membrane and capable of binding an ANT ligand and separable from the fusion protein by cleavage with the protease, wherein the ANT polypeptide comprises an amino acid sequence that is at least 95 percent identical to a human ANT3 sequence as set forth in SEQ ID NO:33.

57. (Amended) The fusion protein of either claim 47 or claim 52 wherein the additional polypeptide sequence is a polypeptide having affinity for a ligand.